REMARKS

Claims 15, 17-23, 26, 32, 34-37, 39, and 40 are rejected. Claims 1-14, 16, 25, 33, and 38 were previously canceled while claims 24 and 27-31 were previously withdrawn. Claims 15 and 26 have been amended while claim 23 has been canceled herein. Therefore, claims 15, 17-22, 26, 32, 34-37, 39, and 40 are pending and at issue. Applicants respectfully request reconsideration of the rejections and allowance in light of the foregoing amendments and the following remarks herein.

Double Patenting

Claims 15, 17-23, 26, 32, 34-37, 39, and 40 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-14 of co-pending Application Serial No. 12/669,781. Applicants respectfully disagree with this characterization of the present claims as well as the claims of co-pending Application Serial No. 12/669,781. Furthermore, the presently amended claims are even further distinguished from those of co-pending Application Serial No. 12/669,781 such that this rejection should be withdrawn. Regardless, Applicants respectfully request that this rejection be held in abeyance until the claims of the present application and/or the claims of co-pending Application Serial No. 12/669,781 are allowed so Applicants may reevaluate this rejection.

The Present Application

The present application is generally directed to a Specific Immunological Extraction Follow by Enzymatic Detection (SIEFED) method and kit. SIEFED measures the enzymatic activity, such as the activity of myeloperoxidase. As discussed throughout the present application, such as at paragraphs [0050], [0051], [0053], [0088], [0107], [0131] and [0134], Applicants have unexpectedly found that by adding nitrite, the detection sensitivity could he enhanced. More specifically, the addition of nitrites enhanced the fluorescence. In one form,

"amplification of the detection signal makes it possible to accurately measure and detect the enzymatic activity of an enzyme, for instance that of MPO originating from neutrophils, in the most complex (biological) media, tissues or samples." See, for example, paragraph [0050] of the present application. In some forms, Applicants have found up to at least a 20-fold increase in the sensitivity of enzymatic detection using nitrite as a fluorescence enhancer.

The Cited Art

The cited art is generally directed to different processes than the present application. For example, Deby et al. is directed to an ELISA. An ELISA measures the total amount of the protein, such as myeloperoxidase. In other words, Deby et al. is directed to detection of myeloperoxidase, not to the measurement of its enzymatic activity. For example, Deby et al. describes at col. 21, lines 37-64 that alkaline phosphatase activity is measured which reflects the total MPO and not the active MPO. Moreover, it is the alkaline phosphatase activity which is measured, not the activity of the bound MPO, such as in the present application.

Uchida et al. is directed to a similar method which measures the amount of protein, such as myeloperoxidase, which is then considered to indicate inflammatory gastrointestinal tract disorders. Just as with Deby et al., Uchida et al. is directed to determining the amount of protein and not the activity of immunocaptured enzyme. Therefore, both Deby et al. and Uchida et al. are directed to entirely different methods and kits than those described in the present application.

Janckila et al. is also directed to a different method and analysis. For example, the method is not specific for the bone tartrate acid resistant phosphatase (TRAcP) which they want to use as a marker of osteoclastic processes. In order to be specific, the method requires an extraction of the sample and to work at two different pH values.

In Janckila et al., an extraction is necessary because there are numerous isoforms of TRAcP in serum, and their purpose is the TRAcP derived from bone and marker of bone degradation. Therefore, Janckila et al. thus need to extract the different isoforms from the

serum before performing the enzyme-capture immunoassay. Nakasato et al. (1999) (page 2151, left column, Antibodies), which was cited in the references section of Janckila et al., write that the monoclonal antibody 14G6 which they use in their immunoassays (two-site immunoassay and enzyme-capture immunoassay) for the TRAcP capture was obtained by immunisation against a TRAP purified from the hairy cell rate (from subjects affected by hairy cell leukemia, a disease characterized by anormal B lymphocytes). This 14G6 antibody recognizes also an epitope present on the TRAP of osteoclasts and macrophages (see Janckila et al. Heterogeneity of hairy cell tartrate resistant acid phosphate, Clin Biochem 1992; 25: 437-443). The 14G6 antibody is thus not specific. The calibrator protein also is a TRAP protein partially purified from hairy cell rate and further purified by affinity chromatography. The enzyme capture immunoassay is performed with this 14G6 antibody (Janckila et al., 2001, page 2151, right column, last paragraph). To reach specificity (distinction between two isoforms), Janckila et al. describe a chromatographic step and a measurement at two different pHs.

Claim Rejections — 35 U.S.C. § 103

Claims 15, 17, 19-21, 26, 32, 34, 36, 37, 39, and 40 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Uchida et al. U.S. Patent No. 5,552,292 ("Uchida et al.") in view of Janckila et al., "Tartrate-resistant Acid Phosphatase Isoform 5b as Serum Marker of Osteoplastic Activity," Clinical Chemistry 47 (1): 74-80 (2001) (Janckila et al.). This rejection should be withdrawn as the cited references fail to disclose or suggest the features recited in the claims.

As discussed above, Uchida et al. and Janckila et al. are directed to different processes compared to the present application and claims and are otherwise not combinable as proposed by the Office Action. For this reason alone, the rejection should be withdrawn.

Furthermore, independent claims 15 and 26 have been amended to include features from claim 23. More specifically, claims 15 and 26 have been amended to include, amongst other features, adding an effective amount of nitrite to the reaction medium to enhance a generated

fluorescent signal. The Office Action implicitly acknowledges that Uchida et al. and Janckila et al. fail to disclose or suggest such features as claim 23 was not rejected in view of these references alone. Therefore, for this additional reason, this rejection should be withdrawn.

Claims 15, 17, 19-21, 26, 32, 36, 37, and 40 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Deby et al. U.S. Patent No. 5,460,961 ("Deby et al.") in view of Janckila et al. This rejection should be withdrawn as the cited references fail to disclose or suggest the features recited in the claims.

As discussed above, Deby et al. and Janckila et al. are directed to different processes compared to the present application and claims and are otherwise not combinable as proposed by the Office Action. For this reason alone, the rejection should be withdrawn.

Furthermore, independent claims 15 and 26 have been amended to include features from claim 23. More specifically, claims 15 and 26 have been amended to include, amongst other features, adding an effective amount of nitrite to the reaction medium to enhance a generated fluorescent signal. The Office Action implicitly acknowledges that Deby et al. and Janckila et al. fail to disclose or suggest such features as claim 23 was not rejected in view of these references alone. Therefore, for this additional reason, this rejection should be withdrawn.

Claims 18, 23, and 35 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Uchida et al. or Deby et al. in view of Janckila et al. as applied to claims 15, 17, 19-21, 26, 32, 34, 36, 37, 39, and 40, and further in view of Wilson et al. U.S. Patent Application Publication 2006/0257879 ("Wilson et al."). As noted above, independent claims 15 and 26 have been amended to include features from claim 23. Therefore, this rejection will be discussed with reference to claims 15 and 26.

This rejection should be withdrawn as all of the cited references, when considered alone or in combination, fail to disclose or suggest one or more features recited in claims 15 and 26, as amended. More specifically, as discussed above, claims 15 and 26 have been amended to recite adding an effective amount of nitrite to the reaction medium to enhance a generated fluorescent signal. None of the references disclose or suggest such features. The Office Action alleges that

Wilson et al. discloses fluorogenic substances for horseradish peroxidase. However, assuming *arguendo* that this characterization is accurate, Wilson et al. fails to disclose or suggest adding an effective amount of nitrite to the reaction medium to enhance a generated fluorescent signal. Therefore, as all of the cited references fail to disclose or suggest one or more features recited in the claims, the rejection should be withdrawn and the claims allowed.

Claim 22 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Uchida et al. or Deby et al. in view of Janckila et al. as applied to claims 15, 17, 19-21, 26, 32, 34, 36, 37, 39, and 40, and further in view of Deby-Dupont et al., "Equine Neutrophil Myeloperoxidase in Plasma: design of a radio-immunoassay and first results in septic pathologies," Veterinary Immunology and Immunopathology 66:257-271 (1998) ("Deby-Dupont et al."). Claim 22 depends from and more specifically recites the features of claim 15. As discussed above, Uchida et al., Deby et al. and Janckila et al. fail to disclose or suggest adding an effective amount of nitrite to the reaction medium to enhance a generated fluorescent signal. Deby-Dupont et al. similarly fails to overcome this deficiency. Therefore, this rejection should also be withdrawn and the claims allowed.

The Commissioner is hereby authorized to charge any additional fees which may be required with respect to this communication, or credit any overpayment, to Deposit Account No. 06-1135.

Respectfully submitted,

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